

REMARKS

The Office Action

Claims 59-69 are pending in this application. Claims 59-69 stand rejected for obviousness-type double patenting.

Rejection for Obviousness-type Double Patenting

Claims 59-69 stand rejected for nonstatutory obviousness-type double patenting as being unpatentable over claims of U.S. Patent Nos. 5,626,863; 5,986,043; 5,567,435; and 5,410,016.

As the Office Action recognizes, none of the claims of U.S. Patent Nos. 5,626,863; 5,986,043; 5,567,435; and 5,410,016 recite a macromer composition comprising at least 5% by weight biologically active substance as required by the pending claims.

Nevertheless, as a basis for this rejection, the Office Action states:

Also, to vary the amount of protein or peptide to be contained by the composition in an amount of 5% by weight of the peptide or protein, as the case might be, is well within the purview of an ordinary artisan.....
Therefore, the patented claimed subject matter would have made obvious the claimed subject matter at the time it was made.

Applicants respectfully disagree.

Applicants assert that making and delivering macromers containing such high percentages of biologically active substance, by weight, is not obvious. As attested to in the enclosed Declaration of Dr. Jeffrey Hubbell, the present claims are not obvious

because they are directed to compositions for delivering biologically active substances, wherein the biologically active substance is at least 5% active substance by weight. According to Dr. Hubbell, historically, it has not been deemed desirable to load macromers with the large amounts of biologically active substance, as claimed in the present invention, because it was believed that increased bursting occurred as the macromers were loaded with increasing amounts of biologically active substance.

To find the invention obvious, the prior art must contain both a suggestion of the modification and an expectation of success.

In moving from the prior art to the claimed invention, one cannot base a determination of obviousness on what the skilled person might try or find obvious to try. Rather, the proper test requires determining what the prior art would have led the skilled person to do. In evaluating obviousness, one must look to see if “the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art.... Both the suggestion and the expectation of success must be founded in the prior art, not in the Applicant’s disclosure.” *In re Dow Chemical Co. v. American Cyanamid Co*, 837 F.2d 469, 5 USPQ2d 1529.

The Examiner’s conclusion of obviousness relies upon improper use of hindsight.

The Examiner presumes that the claimed compositions and prior art compositions, being similar, are expected to have similar properties. The Examiner's rejection relies upon this presumption to find both the requisite suggestion and expectation of success in the prior art. However, this presumption is only valid if one skilled in the art would have recognized, at the time of the invention, that the claimed compositions were expected to have the same properties as the prior art compositions. It is improper to conclude that because the controlled release rates of the prior art compositions and those of the claimed invention are the same that they were expected to be the same at the time of the invention. To do so is to hold the Applicant's own disclosure, in hindsight, against the patentability of the Applicant's own claims. Rather, the Examiner must determine what the prior art, at the time of the invention, would have suggested to one skilled in the art about the use of at least 5% biologically active substance in the Hubbell macromer. At issue is whether one skilled in the art would have expected, at the time of the invention, that the claimed compositions would have desirable controlled release properties. Applicant asserts that one skilled in the art would not have expected desirable properties for the reasons described below.

One skilled in the art would have expected undesirable release properties (burst) from the claimed compositions.

To achieve the release of therapeutically useful levels of biologically active substance, it is desirable to maximize the loading of the macromer. While this was true

prior to the time of the instant invention, there is no record in the prior art of the preparation of, or the desire to prepare, a Hubbell macromer containing at least 5% biologically active substance. Those skilled in the art, including Hubbell himself, were not motivated to prepare the claimed compositions because they believed that increasing the amount of biologically active substance would exacerbate the problem of burst. *See* Hubbell Decl. ¶ 4. Burst is a highly undesirable feature in sustained release compositions because the goal of such compositions is to deliver a steady, even, amount of drug over the appropriate time period. Furthermore, for some therapeutics, burst may result in adverse side effects. The claimed compositions had not been previously prepared because those skilled in the art expected these compositions to have undesirable release properties. Accordingly, the expectation of success, a required element of the Examiner's case of *prima facie* obviousness, is missing and the rejection should be withdrawn.

U.S. Patent No. 5,410,016 teaches away from a higher loading of the macromer.

The examples provided in U.S. Patent No. 5,410,016 indicate that increased bursting occurs when the Hubbell macromers are loaded with increasing amounts of biologically active substance. Specifically, in a macromer loaded with 0.1% BSA, the BSA was released from the macromer without bursting (see Figure 3A of Hubbell '016). In contrast, in a macromer loaded with 3.3% lysozyme, the lysozyme exhibited burst as 25% of the lysozyme was released at 24 hours (see Figure 3B of Hubbell '016).

Accordingly, Hubbell '016 teaches away from the claimed invention. More importantly, Hubbell '016 fails to suggest of the desirability of increasing the amount of biologically active substance in the macromer. A suggestion of the claimed modification is a required element of the Examiner's case of *prima facie* obviousness. This element is missing and the rejection should be withdrawn.

Finally, Applicant notes that the courts have repeatedly recognized that proceeding contrary to the accepted wisdom in the art represents "strong evidence of unobviousness." See *In re Hedges*, 783 F.2d 1038, 228 USPQ 685 (Fed. Cir. 1986); *WL Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983); and *In re Fine*, 837 F.2d at 1074, 5 USPQ2d at 1599 (Fed. Cir. 1988).

For these reasons, and in view of the Declaration of Dr. Hubbell, Applicant believes that the presently claimed invention is not obvious over the claims of U.S. Patent Nos. 5,626,863; 5,986,043; 5,567,435; and 5,410,016. Applicant respectfully requests that the rejection of the present claims for obviousness type double patenting be withdrawn.

CONCLUSION

Applicants respectfully submit that the pending claims are in condition for allowance. If an interview with Applicants' attorney would expedite prosecution, the Examiner is invited to call the undersigned at 617-428-0200.

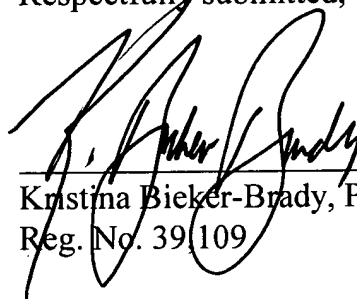
Enclosed is a Petition to extend the period for replying to the Office action for three months, to and including March 19, 2007, and a check in payment of the required extension fee.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date:

March 19, 2007



Kristina Bieker-Brady, Ph.D.
Reg. No. 39,109

Clark & Elbing LLP
101 Federal Street
Boston, MA 02110
Telephone: 617-428-0200
Facsimile: 617-428-7045